UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/263,626	03/05/1999	PAUL A. MOORE	PF466	2059

22195 7590 01/13/2004

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/263,626	MOORE ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-50,60-98,100-124,126-131,133-150,154 and 155* is/are pending in the application.

4a) Of the above claim(s) *40,76 and 83-98* is/are withdrawn from consideration.

5)☐ Claim(s) *39,41,78-82 and 133-139* is/are allowed.

6)☐ Claim(s) *25-38, 42-50, 60-75, 100-124, 126-131, 140-150, 154, 155* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 2/28/03, have been entered in full.

Applicant's election (received 6/16/03), with traverse, of the species of polynucleotide encoding a peptide of consisting of amino acid residues 1-231 of SEQ ID NO: 2 is acknowledged. Applicant asserts that claims 37, 39, 77, 81, 129-131, 140-141, 143-150 and 154-155 read on the elected species. The examiner finds that claim 38 also reads on the elected species. Further, the examiner deems it necessary to search SEQ ID NO: 1, and thus claims 25-40, 42-50, 60-75, 77, 81, 100-150, 154 and 155 will also be examined in this Office action. Additionally, because generic claim 39 has been found allowable, dependent claims 78-82 will be examined in this Office action, 37 CFR 1.142(b). The examiner finds that claims 40, 76, 83-98 do not correspond to the elected species. Further, a search of the elected species and of SEQ ID NO: 1 could not be relied upon to provide art that is either anticipatory or might render obvious claims 40, 76, 83-98. To make all of the searches required to examine these claims in a single application would be burdensome. Therefore, claims 40, 76, 83-98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant asserts that if the examiner finds such subject matter allowable, then the other non-elected species will examined. This assertion is not correct. The species identified by the examiner are independent and distinct inventions, as indicated in the previous office action. Only upon the allowance of a generic or linking claim, would the other species be searched, see

MPEP 809. Applicant argues that because the examiner had indicated that claims 40, 76, 78-80, and 82-98 are generic, then pursuant to MPEP 809.02, these claims must be examined. This argument has been fully considered but not deemed persuasive. These claims are not generic to the elected species, i.e. they are generic to other species but do not encompass the elected species. Never-the-less claims 78-82 will be examined because generic claim 39 was found to be allowable.

Applicant's arguments regarding the distinction between the fragment consisting of 1-231 and 23-225 are persuasive. Thus, the claims will also be examined with respect to residues 23-225 of SEQ ID NO: 2.

Applicant argues that the examiner is requiring an election of the members of Markush type claims, and thus, a reasonable number of species must be examined if the elected species is free of the prior art. This argument has been fully considered but not deemed persuasive. While Applicant is free to structure claims in a variety of formats, the fact remains that the application contains claims to patentably distinct inventions, a search of all of which in a single application would be unduly burdensome for the reasons set forth in the previous Office action. Applicant's assertions regarding the search burden involved with searching specific fragments of a protein are incorrect. Each recited fragment requires its own search, and to search all would be burdensome. Therefore the restriction requirement is deemed to be proper, is maintained and made FINAL.

Response to Amendment:

Applicant is notified that any remaining rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

New Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-36, 60-75, 77, 99-131 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite because they either recite or depend from a claim encompassing a polypeptide which "transduces immune cell proliferation". The word "transduce" does not appear to be an art accepted term as it is used in the claims and is therefore indefinite. The word "transduce" is commonly understood to mean: to convert (as energy or a message) into another form, or To bring about the transfer of (as a gene) from one microorganism to another my means of a viral agent. An artisan would not know what lays in between or outside of the bounds of the claims because of this term. For the purpose of this examination, however, the term and the phrase are taken to mean that the presence of the polypeptide stimulates the proliferation of immune cells.

Maintained Rejections:

Claims 25-38, 42-50, 60-75, 77, 99-131, 140-150, 154 and 155 stand rejected 35 U.S.C. § 112 first paragraph, as set forth in item 3 of Paper 22, 4/22/02, in item 7 of Paper 15, and as set forth in item 7, beginning at the second paragraph, and in item 10 of Paper 11 (8/29/00) and

recast below in light of Applicant's amendments and arguments. Specifically, because the claims are not enabled in their full scope, i.e. the specification, while being enabling for a polynucleotide encoding a polypeptide of SEQ ID NO: 2 and for polypeptides consisting of fragments of SEQ ID NO: 2 useful for the production of antibodies specific to SEQ ID NO: 2, and for polynucleotides that specifically hybridize to a polynucleotide of SEQ ID NO: 1, does not provide enablement for polynucleotides *comprising* only portions of SEQ ID NO: 1 nor for polynucleotides encoding polypeptides that *comprise* only portions of SEQ ID NO: 2 or that consist of small portions encoding SEQ ID NO: 2 but are not useful for raising specific antibodies or for specific hybridization, and nor for polynucleotides encoding polypeptides having any recited degree of homology to SEQ ID NO: 2 or for any variants of SEQ ID NO: 2 .

As set forth previously, assuming that one skilled in the art would understand that the instant receptor is expressed in activated T-cells as opposed to resting T-cells, then it is reasonable to also assume that one of skill in the art could use polynucleotides of SEQ ID NO: 1 as hybridization probes to detect activation of T-cells. Similarly, it is reasonable to assume that the skilled artisan could use the polypeptides of SEQ ID NO: 2 to raise antibodies useful for the detection and/or isolation of activated T-cells. However, the claims encompass a virtually limitless number of polynucleotide variants of SEQ ID NO: 1. It is reasonable to assume that many of the encompassed polynucleotides could be used as hybridization probes that are specific to SEQ ID NO: 1 such that detection of activated T-cells could be achieved, yet the claims are not so limited to hybridization probes and the specification has failed to teach how to use other claimed polynucleotides that could not be used as probes for SEQ ID NO: 1. Of those polynucleotides that may not be useful as probes, it can be expected that only a small number

will encode a polypeptide of SEQ ID NO: 2 due to the degeneracy of the genetic code. This small number is enabled. However, polynucleotides encoding variants of SEQ ID NO: 2 are not enabled, as set forth previously, particularly at page 6 of Paper 6 (1/3/00) and on page 8 of Paper 11 (8/29/02). Applicant's arguments regarding enablement for polynucleotide variants of SEQ ID NO: 1 have been substantially addressed previously in Papers 6 and 11.

Further, claims 37, 38, 77 (and dependent claims) have been amended to consist of a genus of polynucleotides encoding only portions of the polypeptide of SEQ ID NO: 2, e.g. claims to polynucleotides encoding dipeptides, tripeptides, etc. are within the scope of the claimed genus, and now make up a substantial portion of this genus. Yet the specification has not provided sufficient guidance as to how to use these small polynucleotides in any productive way, i.e. the specification has not taught which of these small fragments, if any, could be used as hybridization probes that could specifically detect a polynucleotide of SEQ ID NO: 1 or to produce a polypeptide that could be used to raise antibodies that specifically bind to a polypeptide of SEQ ID NO: 2. It is well appreciated in the art that polypeptides of at least 7 contiguous amino acids are required to produce specific antibodies; this is essentially admitted to on page 24, lines 27-29 of the instant specification

Applicant argues that that is was agreed during the Interview (Paper 26) that polynucleotides encoding fragments of the disclosed sequences are enabled. However, the examiner finds that the instant amended claims contain a substantial subgenera that would not be useful as either probes or in the production of antibodies, as explained above. Applicant additionally argues that fragments would also be useful for transducing immune cell proliferation. This argument has been fully considered but not deemed persuasive. With regard

to the small fragments referred to above, there does not appear to be any assertion that such fragments would be useful to "transduce immune cell proliferation", although it may not have been Applicant's intention to argue that case. Never-the-less, the specification has failed to provide sufficient teaching regarding the transduction of immune cell proliferation using any of the disclosed polypeptides or polynucleotides. Applicant's post-filing date research on the subject, as referred to in the Declarations, does not provide evidence that any particular assertions that were made in the application were correct, because no *particular* assertions were made, e.g. the locations in the specification pointed to by Applicant e.g. page 1, 45, 56 and 58 simply present a laundry list of known immune cell types and disorders. The skilled artisan would recognize that it would require extensive trial and error experimentation, some of which are described in the Declarations, to find how to particularly use any of the polynucleotides so as to "transduce immune cell proliferation".

Applicant's arguments regarding the Declarations have been substantially addressed previously. Particularly the Declaration of Thi-Sau Migone, demonstrate that CRCGCL binds the cytokine TSLP. This argument has been fully considered but not deemed persuasive; the issue, as discussed previously, is that CRCGCL (alone) would not be expected to regulate the differentiation and/or proliferation of cells as is required by claims. In fact, analogous to the known activity of Interleukin-2 receptor gamma which requires IL-2 receptor alpha and or beta subunits, Reche et al., teach that a functional complex involving the instant CRCGCL requires the involvement of IL-7R and TSLP (see page 338, col 2, Identification of a functional heteromeric human TSLP receptor complex). The instant specification says nothing about TSLP; the specification directs the skilled artisan to search for binding of a multitude of

cytokines but does not mention TSLP (see page 85, lines 20-28). Additionally, the specification does not guide the skilled artisan to use the instant polypeptides in conjunction with any IL receptor alpha chain, much less provide guidance to use the IL-7R . Further, the specification asserts that preliminary data indicates that the instant polypeptides interact with Jak1 (see page 86, line 1) whereas the Declaration filed under 37 CFR 1.132 filed as Paper 14, 2/27/01 indicates that Jak2 is involved and says nothing about Jak1. Thus, the specification does not provide adequate guidance to produce a polypeptide of SEQ ID NO: 2 that either promotes or inhibits the differentiation and/or proliferation of cells as is required by claims.

Applicant argues that the Moore Declaration of 2/27/01 demonstrates that the claimed invention binds a cytokine and promotes cell proliferation and an extracellular soluble fragment could inhibit such proliferation. This argument has been fully considered but not deemed persuasive. The examiner can find no evidence in the Moore Declaration of any effect on cell proliferation, particularly not immune cell proliferation as required by the claims. The Moore Declaration describes phosphorylation experiments in transfected human embryonic kidney cells, not in immune cells and no effect on proliferation was even looked for in these experiments. More importantly, the experiments referred to therein rely on the use of TSLP, IL7R and Jak2. As set forth above, there is no mention of TSLP, nor of IL-7R in the instant specification. Further, the instant specification would lead the artisan to looked to Jak1 and not Jak2 (see page 86, line 1).

Applicant argues that the Moore declarations of 2/27/01 and 2/27/03, establish that SEQ ID NO: 2 can bind a cytokine alone as well as when cotransfected with the IL-7R chain. This argument has been fully considered but not deemed persuasive. That low affinity binding can be

detected by FACS analysis, as in the Moore Declaration, in no way leads to the expectation that this low affinity binding would have any effect on immune cell proliferation; this is affirmed by Leonard, W. Nature Immunology, 3(7)605-607, 2002, who reviews the art and concludes that the IL-7R is an essential component of the TSLP receptor [emphasis added] (see page 606, col 1, second full paragraph). Leonard also concludes that "human TSLP does no appear to have direct biological effects on B-cells, T-cells, natural killer cells, neutrophils or mast cells"., see page 606, col 3 first paragraph. The instant specification has simply presented a laundry list of possible cell types (including B-cells, T-cells, natural killer cells, neutrophils and mast cells) and possible effects that the instant polypeptide might be involved in. The artisan, however, is then required to undergo an extensive research plan to determine which particular cell types could be manipulated and also to determine what type of manipulations are possible; this does not constitute enablement for the claimed requirements of "transducing immune cell proliferation" or "inhibiting immune cell proliferation", and nor has the scope of that which is being claimed been validated by post filing-date research that has been cited, above, by both the Applicant and the examiner.

Claims 25-36, 42-50, 60, 75, 77, 99-131, 140-150, 154 and 155 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, as set forth previously in item 11 of Paper 15, and recast below in view of Applicant's amendments and arguments.

The specification discloses a polynucleotide of SEQ ID NO: 1, yet the claims encompass polynucleotides not described in the specification, e.g., sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification. Further, the claims require a large subgenus of small fragments that either "transduce immune cell proliferation" or "inhibit immune cell proliferation". There is no description of such, and nor could it be reasonably inferred that Applicant was in possession of such at the time of filing.

With the exception of the of the polynucleotide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants or fragments that have any particular recited activity toward immune cell proliferation Therefore, only the polynucleotide of SEQ ID NO: 1, and polynucleotides *consisting* of fragments thereof, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Citing case law, Applicant argues that each and every compound need not be expressly named to comply with the written description requirement, and that the specification contemplates variants and fragments of the claimed invention. This argument has been fully considered but not deemed persuasive. Simply verbalizing that variants are contemplated does not put one in possession of the variants any more than does verbalizing "a book written in English" put one in possession of any particular book. Similarly, simply verbalizing that

fragments inhibit proliferation or transduce proliferation does not put one in possession of any fragments that do inhibit proliferation or transduce proliferation.

Allowable Subject Matter

Claim 39, 41, 78-82, 133-139 are allowed.

Conclusion

Please note the new official fax number below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 31, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER